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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/127,411	07/31/1998	MICHEAL L. GRUENBERG	24731-500C	1111

25225 7590 11/19/2003

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/127,411	GRUENBERG, MICHEAL L.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-40,154,160,161,163-167,170,171,174,175 and 177* is/are pending in the application.

4a) Of the above claim(s) *39,40,154 and 171* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,38,160,161,163-167,170,174,175 and 177* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Applicant's election with traverse of the species antiCD3 and antiCD28, and methods that employ IL-12 in the papers filed 2/7/2003 and 8/28/2003 is acknowledged. The traversal is on the ground(s) that are stated in said papers. This is not found persuasive because of the following reasons. The method of claim 37 encompasses a method that uses a) antiCD3 antibody or b) antiCD28 antibody or c) antiCD3 and antiCD28 antibody. The antiCD3 antibody and antiCD28 antibody recognize different proteins that are functionally and structurally distinct. The antiCD3 antibody, antiCD28 or mixtures of said antibodies each have different physiologic mechanisms and properties.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 39,40,154,171 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the papers filed 2/7/2003 and 8/28/2003.

3. Claims 37,38,160,161,163-167,170,174,175,177 are under consideration. Claims 162,168,169,172,173,176 have been cancelled. Claims 37,38 have been amended.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 37,38,160,161,163-167,170,174,175,177 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification for the recitation of "collecting mononuclear cells" in the context recited in claim 37. The original claims disclose the

claimed method wherein the claim recites "isolating CD4+ mononuclear cells", but not the claimed invention which recites "collecting mononuclear cells". The claimed method encompasses contacting unfractionated cells with antibody and then selecting CD4 positive cells, but said method is not disclosed in the specification as originally filed wherein said cells are obtained from an HIV infected patient. There is no disclosure in the specification as originally filed of the scope of the claimed invention (eg. it constitutes new matter).

Regarding applicants comments, the specification, pages 28 or 29 do not refer to the claimed method (eg. expansion of virally purged Th1 cells). The original claims disclose the claimed method wherein the claim recites "isolating CD4+ mononuclear cells", but not the claimed invention which recites "isolating mononuclear cells". There are numerous different methods disclosed in the specification which use different steps. Examples 1 and 2 in the specification are not drawn to the scope of the claimed invention (eg. they refer to methods involving normal cells, not expansion of virally purged Th1 cells). Regarding Example 3 in the specification, said Example discloses that mononuclear cells were collected, then the CD4+ cells were isolated and the isolated CD4+ cells were activated with antibody and IFN-gamma. Thus, the contacting step with antibody is not performed until after CD4+ cells have been isolated. The claimed method encompasses contacting unfractionated cells with antibody and then selecting CD4 positive cells, but said method is not disclosed in the specification as originally filed wherein said cells are obtained from an HIV infected patient.

6. Claims 37,38,160,161,163-167,174,175,177 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the

specification does not convey to the artisan that the applicant had possession at the time of invention of the invention as recited in the claims.

The instant claims encompass a method that uses an agent to induce T cells to differentiate into Th1. However, the only specific agents to induce Th1 differentiation disclosed in the specification are treatment with antiIL-4 antibody or interferon gamma or IL-12 or antiIL-12 receptor antibodies. The claims encompass use of a potentially vast array of undisclosed agents in the claimed method. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. In the instant case, the facts are similar to those disclosed in University of California v. Eli Lilly and Co. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated:

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

7. Regarding priority for the claimed inventions with regards to the application of prior art, the claimed inventions are not disclosed in parent application provisional application 60/044693 (the application formerly known as 08/506668), and therefore priority with regards to the application of prior art is taken as the filing date of parent application 08/700565 to which applicant claims priority. The claimed method lacks description in parent application provisional application 60/044693 for the same reason that the claimed invention constitutes new matter as per paragraph 5 of this Office Action. In addition, there is disclosure of the use of "mitogenic antibodies" in parent application 60/044693, which is restricted to the use of mitogenic monoclonal antibodies.

Regarding applicants comments, the only disclosure of a method for producing virally purged Th1 cells in parent application 60044693 is Example 2. Said example is not of the scope of the claimed invention (eg. it is limited to use of a particular method for purifying starting cells, wherein said cells are stimulated with two particular antibodies (antiCD3 and antiCD28) and interferon-gamma in a particular series of steps). Applicant has referred to various parts of the parent application that refer to methods other than the claimed method. Applicant appears to be arguing that the claimed method is obvious based on other methods disclosed in the specification. However, obviousness is not the appropriate standard with regards to issues of written description. The CAFC stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1997) that:

3. Patentability/Validity -- Specification -- Written description (§ 115.1103) Patent's entitlement to earlier filing date extends only to that which is disclosed in prior application, and does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed; one shows that one is "in possession" of invention of patent by describing invention, with all its claimed limitations, not that which

makes it obvious, and although prior application need not describe claimed subject matter in exactly same terms used in claims, prior specification must contain equivalent description of claimed subject matter, and description which renders obvious invention for which earlier filing date is sought is not sufficient.

The CAFC also stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) that:

The invention is, for purposes of the 'written description' inquiry, whatever is now claimed .") (emphasis in original). One does that by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. Although the exact terms need not be used in haec verba , see Eiselstein v. Frank , 52 F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995) (" [T]he prior application need not describe the claimed subject matter in exactly the same terms as used in the claims.. . ."), the specification must contain an equivalent description of the claimed subject matter. A description which renders obvious the invention for which an earlier filing date is sought is not sufficient.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 37,38,160,161,163,164,170,174,175,177 are rejected under 35 U.S.C. § 103 as being unpatentable over June et al. (US Patent 6,352,694) in view of O'Garra et al., Seder et al. and Carew (US Patent 5,123,901).

June et al. teach that Th1 cells can be produced and expanded using treatment of CD4+ T cells with antiCD3 antibody and antiCD28 antibody (see column 30, penultimate paragraph). Said method does not use exogenous IL-2. June et al. teach that the CD4+ cells used can be antigen specific (see column 30, first complete paragraph). The antiCD3 and antiCD28 antibodies taught by June et al. are mitogenic monoclonal antibodies (see Example 14). The cells can be further isolated or purified

(see column 19). The starting material can be human T cells isolated from PBL (see column 19). The cells can be expanded to reach greater than 10^{10} cells (see column 28, lines 1-5 and column 54). The cells are homogenous because June et al. teach that this method selectively expands Th1 cells (see column 30, penultimate paragraph). The antiCD3 and antiCD28 antibodies can be monoclonal antibodies (see column 5, last paragraph and column 7, first paragraph). June et al. teach that the cells can be from an HIV infected patient (see column 28, first paragraph). June et al. disclose that the antiCD3/antiCD28 treated cells are essentially HIV negative (see Example 16). June et al. do not disclose that the cells are in the volumes recited in the claims or that the CD4+ cells are separated after activation or the use of IL-12 in said method. Seder et al. teach that Th1 (eg. interferon gamma producing cells derived from CD4+ T cells) can be produced by treating CD4+ cells with IL-12 (see abstract) or interferon gamma (see page 10190, second column, last paragraph, first sentence). O'Garra et al. teach that Th1 can be produced by treating CD4+ cells with IL-12. Carew teaches that HIV positive T cells can be removed from blood or a fluid containing said infected cells by treatment with immunoreactive beads coated with a reagent that binds HIV (see Abstract and column 2, last paragraph). A routineer would have prepared said cells at any desired concentration for administration in vivo in humans. In view of the fact that the cells would be administered to humans, the cells would be checked for HIV positivity at various points in the culture process. June et al. disclose that the cells would be expanded in multiple flasks (see column 53). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because June et al. teach that Th1 cells can be produced and expanded using treatment of CD4+ T cells with antiCD3 antibody and antiCD28 antibody wherein said method does not use exogenous IL-2 while Seder et . and O'Garra et al. teach that Th1 can be produced by treating CD4+ cells with IL-12 and Carew teaches that HIV positive T cells can be removed from blood or a fluid containing said infected cells by treatment with immunoreactive beads coated with a reagent that binds HIV. One of ordinary skill in the art would have been motivated to do the aforementioned because June et al. teach that the presence of TH1 specific cytokines in culture cause the enrichment in TH1 (see column 30, penultimate paragraph). One of ordinary skill in the art would have been motivated to do the aforementioned because June et al. teach a variety of uses for expanded T cell subsets and because Carew

teaches that HIV infected T cells should be removed from blood products that are administered to humans (see abstract).

10. Claims 165-167 are rejected under 35 U.S.C. 103(a) as being unpatentable over June et al. (US Patent 6,352,694) in view of O'Garra et al., Seder et al. , Carew (US Patent 5,123,901) as applied to claims 37,38,160,161,163,164,170,174,175,177 above, and further in view of Cracauer et al. (US Patent 4,804,628).

The previous rejection renders obvious the claimed method except for use of a hollow fiber reactor. Cracauer et al. teach hollow fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro (see columns 1-3). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection render obvious the claimed method except for the use of a hollow fiber bioreactor and Cracauer et al. teach hollow fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro. One of ordinary skill in the art would have been motivated to do the aforementioned because Cracauer et al. teach that "hollow fiber culture devices have been proven to be ideal for the maintenance of many types of cells at high densities in culture."(column 1).

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644

[illegible]
PRIMARY EXAMINER
GROUP 1800 1600